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Stubborn Challenges Remain With Hepatitis C, Rice Says

BY RICH MCMANUS

There is a difference in public health between being remarkably successful and truly effective, and perhaps no virus illustrates that chasm better than hepatitis C.

In the 27 years since NIH's Dr. Harvey Alter helped identify HCV as the cause of a mysterious form of post-transfusion hepatitis, diagnostics have been created that have made the U.S. blood supply safe from HCV and drugs have been developed that can cure, through elimination of the virus from the body, more than 95 percent of cases.

"That's quite a trajectory," said Dr. Charles M. Rice of the Rockefeller University, who gave the George Khoury Lecture June 8 at NIH. But 100 percent eradication of HCV remains a stubborn challenge, he said. Rice believes a vaccine will ultimately be needed to nail that last 5 percent of the problem.

Dr. Charles M. Rice of Rockefeller University

Further complicating the HCV picture is that most cases are undiagnosed. "Only about 10 percent of patients with HCV in the U.S. have been cured," Rice said. "That's not a very good track record." An estimated 170 million people in the world are infected with HCV.

Also, treatment prices are high (but coming down) and some HCV patients also have liver cancer, cirrhosis and HIV infection. Rice believes, but cannot yet prove, that chronic liver inflammation produced by HCV causes liver cancer.

"A vaccine may be necessary to completely eradicate HCV," he said. "The vaccine work has lagged behind clinical therapies."

Even when a vaccine is available, as has been the case since 1982 for hepatitis B, some 240 million people remain chronically infected with HBV, Rice reported; the ethos of "if you build it, they will come" doesn't necessarily apply to public health challenges.

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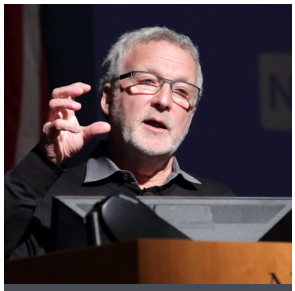
Grooving with ARRA behind Bldg. 10, see p. 12

ALSO THIS ISSUE

Cell Transplants Could Treat Chronic Pain Caused by Nerve Damage

BY ERIC BOCK



Dr. Allan Basbaum

The best treatment for neuropathic pain, that is, chronic pain caused by nerve damage, only works in 30 percent of patients, and at best a 30 percent reduction of pain is typical, said Dr. Allan Basbaum at a recent Wednesday Afternoon Lecture in Masur Auditorium.

"There are a lot of people being under-medicated. They are being treated, but nothing is working, regardless of what they are trying," said Basbaum, professor and

SEE **PAIN**, PAGE 6

An attendee tries out a handheld point-of-care device that determines an individual's eyeglass prescription.

Symposium on Point-of-Care Devices Shows How Far We've Come

BY JESSICA MEADE

Point-of-care devices have helped doctors diagnose and manage diseases for years, giving them the ability to quickly and inexpensively manage diabetes, find out if their patients have a bacterial infection and need antibiotics or are pregnant. Now,

SEE **DEVICES**, PAGE 8

Metro Plans 'SafeTrack' Work on Red Line During August

In August, Metro's Red Line will experience its first phase of SafeTrack construction. Many NIH commuters who take Metro to work will feel the impact, if they haven't already. SafeTrack is an accelerated work plan to address safety recommendations and rehabilitate the Metrorail system. The multi-phase project began June 4 and will be completed by March 2017.

During Aug. 1-7, the Takoma to Silver Spring stations will undergo continuous single tracking, which will result in fewer trains going in both directions across most of the Red Line. This will create longer wait times at stations and more crowded trains.

The greater impact to NIH commuters will occur Aug. 9-18, when single tracking will take place between Shady Grove and Twinbrook stations. During this phase, trains will only serve Shady Grove and Rockville stations every 18 minutes. For more information on the impact to your Metro commute, visit www.wmata.com/rail/safetrack.cfm.

The Office of Human Resources encourages both supervisors and employees to proactively explore whether workplace flexibilities such as compressed work schedules, flexible work schedules and telework may alleviate transportation issues. For more information about work schedule flexibilities, visit https://traffic.nih.gov/Pages/workschedule.aspx.

The Office of Research Services' Division of Amenities and Transportation Services has been reaching out to registered Transhare Program employees to alert them of the surges based on self-reported commutes through Transhare applications. Through these targeted emails, DATS has been and will continue to provide affected employees with additional commuter options and information about workplace flexibilities.

For more information on SafeTrack and strategies to manage your commute, visit https://traffic.nih.gov/Pages/default.aspx.

HHS Launches Demographic Survey

HHS launched a department-wide survey on July 20 to update federal employee records on race, ethnicity and disability status. The Office of Management and Budget and the U.S. Census previously updated the categories for race and ethnicity; HHS is conducting this survey to ensure that it has accurate and up-to-date demographic information for employees within the department.

Currently, NIH and other agencies within the department do not have updated information for employees who were onboard prior to changes in OMB and Census standards. These changes include the ability to identify with more than one racial category, separation of the Asian and Pacific Islander racial categories, addition of a racial category for Native Hawaiian and Other Pacific Islanders and the option to identify ethnicity (Hispanic/Latino) and race.

The survey will also provide an opportunity to update the disability status of employees. Employees may develop disabilities throughout the course of their careers that did not exist when they entered the workforce.

Federal employees will receive an email from HHS with a link to the survey. Employees are asked to take 5 minutes to participate in this voluntary survey. The survey is open for 1 month.

Questions about the survey should be sent to PiSurvey@hhs.gov.

To learn more about NIH efforts in advancing diversity and inclusion, visit the Office of Equity, Diversity, and Inclusion online at http://edi.nih.gov/.

Event Brings Caribbean Flavor to NIH

At the 9th annual Taste of the Caribbean on July 6, two restaurants, the Taste of the Caribbean and Sunrise Caribbean Restaurant, served favorites such as curry goat and shrimp, jerk chicken and rice and beans to hungry NIH'ers. The event was held on the Bldg. 31A patio. Several vendors were also on hand. The lunch was sponsored by the Caribbean Association at NIH and the R&W Association, in partnership with the Caribbean American Chamber of Commerce of the Greater Washington Area Network and Reginald F. Lewis Museum of Maryland African-American History and Culture.

PHOTOS: ERIC BOCK

NIH Supply Center Offers Services

Are you running low on supplies and space in your office? The NIH Supply Center offers services such as standing orders for interval deliveries with less paperwork and the "buy bulk and store" program where supplies are stored in the SC warehouse at no added cost.

As the final quarter of FY16 begins, stop by the Self Service Stores in Bldg. 10 (B2-B41) and Bldg. 31 (B1-A47) to see the enhancements the stores have made to make buying easier.

There are also ways to purchase supplies online. Along with the SC catalog in NBS, you can now place orders through the Purchasing Online Tracking Systems. All institutes now have access to the SC catalog.

Check out the new product catalog at https://nihsccatalog.od.nih.gov. To fax an iProcurement order form, send your order to (301) 402-8493.

Despite Progress in War On Cancer, Access to Care Complicates Efforts

BY COLLEEN LABBE

The ongoing war on cancer has made some inroads, but certain factors, especially disparities in access to care, have tempered our success, according to Dr. Otis Brawley, chief medical and scientific officer for the American Cancer Society. Also an epidemiologist and practicing oncologist, he spoke about the last 50 years of efforts to defeat cancer at the recent NIAMS intramural research program annual scientific training event.

In the mid-20th century, the push to enhance cancer research culminated in enactment of the National Cancer Act of 1971. The law allowed for a significant boost in cancer research spending, better coordination among researchers and improved cancer control and prevention efforts. Brawley explained that cancer-related deaths peaked in 1991 at 215 per 100,000 people. By 2012, cancer deaths had declined by 23 percent. The reduction is largely related to smoking and tobacco use cessation efforts, but it is also correlated with better prevention and early screening efforts, increased cancer awareness and improved treatments. Still, even as the death rate declines, some populations aren't experiencing the same benefits. Why are certain groups doing worse than others?

In public health, stratifying ourselves by race or ethnicity is inherently problematic, because "race does not define biology," Brawley said. Rather, racial constructs are sociopolitical and heterogeneous and their definitions change over the years. The reason that some populations have fared better than others, he said, is because of unequal access to adequate care.

Looking at different types of cancer helps illustrate the access-to-care issue. For instance, in the 1970s, there were no racial differences in deaths among women due to breast cancer. Since 1981, breast cancer deaths have been declining overall. However, mortality rates among white women are dropping more quickly than among black women, presumably due to differences in access to care.

Population differences are seen in deaths

Dr. Otis Brawley (l), chief medical and scientific officer for the American Cancer Society, and Dr. John O'Shea, scientific director at NIAMS

PHOTO: RICH CLARK

associated with colon cancer, as well. The death rate from colon cancer overall has been cut nearly in half since 1975, largely due to early screening, awareness and better treatments. But some states have higher rates of death due to colon cancer than others. "I don't think people in one state are biologically different from those in another state," Brawley said. In addition, when comparing colon cancer patients who have private insurance to patients with Medicaid or no insurance, those with private insurance were more likely to be alive 5 years after diagnosis than those without.

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"We need to realize that adequate health care is a human right."

-DR. OTIS BRAWLEY

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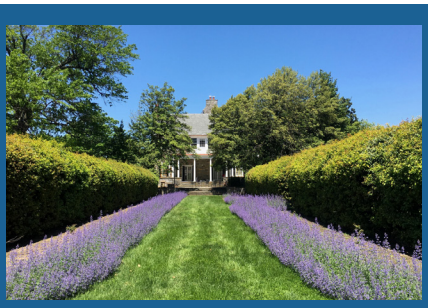
Education can also reduce cancer deaths—people with college degrees are more likely to do better after being diagnosed than those without degrees. Education may also help lessen the coming "tsunami of chronic disease." Obesity and other chronic conditions, said Brawley, will surpass tobacco use as the leading causes of cancer over the next two decades.

Even as we grapple with disparities in access to adequate care, we are in the midst of change involving how we treat cancer—changes that are and will continue to lead to newer and better treatments. We are shifting away from the traditional definition of cancer as a disease involving uncontrolled cell growth and moving toward a better understanding of cancer's molecular basis and genetic influences. This has led to innovative treatment ideas. For instance, we know that cancer cells can evade our typical immune system response by sending a misleading signal and we are learning that certain drugs can override that signal and trigger our immune cells to attack the cancer.

Overall, we have been effective in reducing cancer deaths, but we need to turn our attention to other factors that are complicating our efforts, said Brawley. We need to focus on preventing chronic diseases and "we need to realize that adequate health care is a human right," he concluded. R



ON THE COVER: *A view of Stone House, where offices for the Fogarty International Center are located. Purple catnip adorns the garden.*

IMAGE: SOMA CHOWDHURY, NIGMS

The NIH Record

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Hepatitis C

CONTINUED FROM PAGE 1

Rice said that although great progress has been made on HCV, "it still has many unanswered questions...and there are excellent experimental systems" for gaining new knowledge.

He reviewed three "what next" scenarios involving: the difficulty of culturing primary HCV isolates; new insights gained from understanding how HCV and other viruses require and manipulate microRNAs; and a new model of immunity and pathogenesis based on an HCV relative found in the Norway rat, which does not enjoy the same sentiment attached to the previous best animal model for HCV studies—the chimpanzee.

Rice says that, with hepatitis C, "you never know what's coming next."

PHOTOS: BILL BRANSON

Rice remains optimistic about a field where he acknowledges "you never know what's coming next." He and colleagues continue analyzing the phenotypes of clinical isolates of HCV and exploring microRNA binding sites that offer hints of a general strategy that viruses employ to infect, replicate and manipulate the host.

He said that next-generation sequencing is revolutionizing virology, allowing scientists to sample the amazing biodiversity of viruses in nature and in particular, the discovery of close relatives of HCV in other animal species, for example horses, bats and rats.

"There are many related viruses out there in nature," Rice concluded. He believes animal hepaciviruses will be useful models for understanding HCV immunology and pathogenesis. "They could be useful models for testing HCV vaccine platforms."

As Francesco Lecce-Chong conducts the NSO, NIH director Dr. Francis Collins, who introduced the program, can be seen at rear capturing the music on his smartphone.

PHOTOS: ERNIE BRANSON

NSO Presents 'Peter and the Wolf' at CRC

On June 22, the Clinical Center atrium—filled with patients, visitors and staff—enjoyed the Russian composer Sergei Prokofiev's musical tale *Peter and the Wolf*, presented by the National Symphony Orchestra.

Each instrument in the orchestra portrayed a different character. Narrating the story was Lesli Foster of WUSA Channel 9 news.

The concert was led by conductor Francesco Lecce-Chong and included soloist David Teie on cello. Also on the bill were Beethoven's *Overture to the Creatures of Prometheus, Op. 43 No. 5* and Dvorak's *Silent Woods for Cello and Orchestra*.

The show marked the NSO's 16th visit to NIH as a part of its Sound Health initiative, which brings orchestra music to area hospitals. The NSO began the initiative at NIH in 2013.

The concert was co-presented by the Foundation for Advanced Education in the Sciences and the Clinical Center. The NSO will return to the Clinical Center Sept. 21 as a part of its ongoing partnership with NIH.

Above at left, Lesli Foster of WUSA Channel 9 news narrates Prokofiev's musical tale *Peter and the Wolf*. At right, the audience crowded not only the CRC atrium, but also multiple levels of the 9-story facility. This was the NSO's 16th visit to NIH as part of its Sound Health initiative.

Dr. Alan Schechter (r) and NIDDK director Dr. Griffin Rodgers

PHOTOS: ERNIE BRANSON

NIDDK's Schechter Feted at All-Day Symposium

Dr. Alan Schechter, who began his NIH career in 1965 at NIAMS, was honored June 27 at a daylong symposium in Lipsett Amphitheater titled "Yellow Berets to Gray Hair: Training Physicians and Non-Physicians for Research Careers." The event recognized his 50+ years at NIH.

Schechter is chief of NIDDK's Molecular Medicine Branch and chief of its molecular biology and genetics section. The symposium highlighted the training of physician and non-physician scientists as exemplified by NIDDK's Laboratory of Chemical Biology (LBC), which was the precursor of the Molecular Medicine Branch.

Nobel Prize recipient Dr. Christian Anfinsen was first chief of the LBC. He was followed by Schechter, who is a leading investigator in hemoglobin structure and function, especially as related to sickle cell disease, and interactions with nitric oxide and circulatory physiology.

For the past five decades in his lab, Schechter's experience and leadership have encouraged an atmosphere of professional development; he has served as a mentor to many scientists. Speakers included former lab trainees and associates and representatives from hematology, genetics and immunology research training programs. The symposium concluded with a panel discussion on training for clinical and basic research.

Joining Schechter (l) at the symposium were (from l) Dr. David H. Sachs of Massachusetts General Hospital, Dr. Stanley I. Rapoport of NIA and Dr. Jay A. Berzofsky of NCI.

Bowles Discusses Innovations to Improve Discharge Planning

Dr. Kathryn Bowles recently presented the first NINR Director's Lecture of 2016. NINR director Dr. Patricia Grady noted that Bowles' research combines both her basic research and clinical knowledge, as well as trends in data science and electronic health records, while focusing on "what comes after we do the research? What happens now? How can we maximize the impact?"

In her talk "Innovations to Improve Discharge Planning," Bowles said her research began as a clinical question about planning for hospital discharge and led to a successful software company that assists health care providers in their decision-making process.

In her roles as director of the Center for Integrative Science in Aging at the University of Pennsylvania School of Nursing and vice president and director of the Center for Home Care Policy and Research at the Visiting Nurse Service of New York, Bowles emphasized that her goal is to "get the right care for the right patients, at the right time, in the right place."

Dr. Kathryn Bowles (l) and NINR director Dr. Patricia Grady

PHOTO: BILL BRANSON

Early in her career, Bowles built on the research of her mentor, Dr. Mary Naylor, who created and tested the advanced practice nurse-led transitional care model with patients at high risk of poor discharge outcomes. To learn whether patients were being referred to "the right care at the right time," Bowles asked a panel of experts to review records for high-risk patients who had not been referred for post-acute care and make their own recommendations. Her research showed that of those classified by the expert panel as "high-priority" for home care—but who did not get care—half had been re-hospitalized after discharge.

Bowles and her team conducted additional research to help identify some of the reasons for the lack of referrals, hoping to build a tool to provide decision-making support for health care providers as they planned for patient discharge. This research led to development of the Discharge Decision Support System.

Working with the University of Pennsylvania's Center for Technology Transfer, Bowles and CEO Eric Heil co-founded a technology company to bring the decision-making tool to market. With a combination of funding from sources such as NINR R01s, SBIR grants and venture capital, RightCare Solutions was launched.

Continuing studies of the electronic decision-making tool have shown that its use helps reduce readmission rates, particularly among high-risk patients. The software is now in use at 34 hospitals in 8 states across the U.S.

Bowles has continued her research into discharge planning, expanding it to include the types of services patients should be referred to upon discharge, interventions for those who refuse referrals and referrals from emergency departments.

The video of her talk is available at https://www.youtube.com/watch?v=zB2dAudmCvA.

Pain

CONTINUED FROM PAGE 1

chair in the department of anatomy at the University California, San Francisco. At the lecture, he summarized his efforts to develop alternative treatments.

Neuropathic pain is different from pain that results from other conditions. A patient with arthritis, for instance, might experience pain. That discomfort is caused by inflammation of tissues that surround a person's joint. If the inflammation can be treated, the pain goes away.

Basbaum defined neuropathic pain as "a disease of the central nervous system." Nerve damage causes pain. To alleviate it, the nerve damage must be treated. Some conditions associated with neuropathic pain are complex regional pain syndrome, trigeminal neuralgia, stroke, spinal cord injury and multiple sclerosis.

There are several treatments, Basbaum said. Examples include topical anesthetics and anticonvulsants used to treat epilepsy. Opioids are generally not particularly effective for neuropathic pain and there are few studies of the utility of cannabinoids. However, even for the most commonly used approaches, the effects are fleeting and may have serious side effects. Oftentimes, nothing can be done if these treatments fail.

Instead of trying to treat symptoms, Basbaum has been working on a different approach: repairing nerve damage through embryonic nerve cell transplants and, more recently, stem cell treatments.

When there's nerve damage, the central nervous system processes pain differently. This results, in part, from a decrease in the normal inhibitory control exerted by a population of neurons that use the chemical gamma-aminobutyric acid (GABA) as its neurotransmitter.

Normally, GABA helps dull the perception of pain. When GABA- expressing neurons are damaged, secondary to the nerve damage, pain doesn't subside and stimuli that are normally not painful, even light touch, can provoke intense pain. This is what makes the lives of patients with neuropathic pain miserable, Basbaum noted. Patients with neuropathic pain also experience spontaneous pain and "it's almost always a burning sensation."

In Basbaum's laboratory, researchers have been transplanting embryonic nerve precursor cells from the brain's cortex—cells that give rise to inhibitory nerve cells—into the spinal cord of a mouse model for neuropathic pain. He said neuropathic pain decreased without side effects in mice receiving the stem cell transplants. Dr. Joao Braz, an associate researcher in his lab at UCSF, has performed most of these studies.

Basbaum (l) chats with audience members prior to his talk.

PHOTOS: ERNIE BRANSON

Basbaum decided to implant the precursor cells into the spinal cord after several of his colleagues at UCSF showed that cortical precursor nerve cells could be coaxed into developing similarly into GABA neurons in the brain. Importantly, one of their studies was conducted in a mouse model of epilepsy. Basbaum thought he might be able to insert the cells into the spinal cord of a mouse because neuropathic pain and epilepsy are both diseases of a loss of inhibitory control in the central nervous system.

There was no guarantee the experiment would succeed because cortical precursor cells normally develop in the brain; there was no evidence that they could survive in the spinal cord. In fact, the cells did survive and integrated into the neural circuitry of the host spinal cord. And most importantly, the integration was functional and could ameliorate pain hypersensitivity in both a traumatic nerve injury and a chemotherapy-induced model of neuropathic pain.

Basbaum's laboratory is also transplanting the GABA-ergic precursor cells into the spinal cord of mutant mice with a chronic itch condition, also associated with loss of GABA-ergic neurons in the spinal cord.

While it's not always thought of as a major clinical problem, chronic itch can be debilitating. Itch can be so severe that some patients actually scratch through skin and bone. Recent results demonstrated that the transplants are, in fact, remarkably effective against chronic itch.

While results from mouse studies are encouraging, Basbaum said it's still too early to say whether transplants will prove successful in human clinical trials. He is now conducting additional studies in which human embryonic stem cells modified to become GABA-ergic neurons are transplanted into the spinal cord of mice. Results of these studies should be published in the near future.

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"Pain is a complex perception that's colored by emotions and experience."

~DR. ALLAN BASBAUM

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In closing, Basbaum emphasized that chronic pain is not merely a process by which injury messages are transmitted from the spinal cord to the brain. Rather, "Pain is a complex perception that's colored by emotions and experience." For this reason, pain management must consider a blend of pharmacological, psychological and, hopefully in the not too distant future, transplant approaches.

"Every individual who suffers from chronic pain is different, so that a comprehensive and multidisciplinary approach to pain management should always be considered," he concluded.

High Levels of Urinary Paracetamol May Impair Male Fertility, Study Suggests

Couples in which the male partner had high levels of paracetamol in his urine took longer to achieve pregnancy than couples in which the male had lower levels of the compound, according to a preliminary study by researchers at NIH.

Paracetamol, also known as acetaminophen, is a non-prescription drug widely used as a pain reliever and fever reducer. It also is one of the compounds produced when the body breaks down aniline, a chemical used to make rubber, pesticides and coloring agents used in food, cosmetics and clothing. The study was published online in *Human Reproduction*.

"At this point, our findings need to be corroborated by future research, and there is no cause for alarm," said Dr. Melissa Smarr, the study's first author, a postdoctoral fellow in the Division of Intramural Population Health Research at NICHD.

Smarr explained that the high levels of paracetamol in the urine of certain men in the study were unlikely to result only from taking medications and were more consistent with those seen from environmental exposure, either to aniline or paracetamol or a combination of the two. The findings could have implications for the amount of paracetamol exposure that is considered acceptable.

The authors stressed that their findings need to be confirmed by larger studies that can better identify the sources of paracetamol, the duration of time the participants are exposed and the amount of the compound to which they are exposed.

Researchers Make Advance in Possible Treatments for Gaucher, Parkinson's Diseases

With assistance from high-throughput drug screening, NIH researchers have identified and tested a molecule that shows promise as a possible treatment for the rare Gaucher disease and the more common Parkinson's disease. Dr. Ellen Sidransky, a senior investigator with NHGRI, and her collaborators at NINDS and NCATS published their findings June 12 in the *Journal of Neuroscience*.

"Until now, drugs used to treat Gaucher disease have not been able to enter the brain and reach those neurons that are affected in the most severe forms of Gaucher disease or in Parkinson's disease," said Sidransky. "It's really exciting to have found a molecule that theoretically could be widely available to treat people with these diseases. However, there's a long distance between identifying this molecule and having an approved drug."

Sidransky has conducted research on Gaucher disease for the last 28 years and made the connection between Gaucher disease and Parkinson's disease in 2001.

"This research constitutes a major advance," said Dr. Daniel Kastner, NHGRI scientific director. "It demonstrates how insights from a rare disorder such as Gaucher disease can have direct relevance to the treatment of common disorders like Parkinson's disease."

Researchers will next test the new molecule to see if it might be developed into an appropriate prototype drug for patients with Gaucher disease and Parkinson's disease.

Gaucher disease affects an estimated 1 in 50,000 to 1 in 100,000 people in the general population. People of Eastern and Central European (Ashkenazi) Jewish heritage are more likely to get Gaucher disease. Parkinson's disease affects 1.5-2 percent of people over age 60, and the incidence increases with age. In the United States, about 60,000 new cases are identified each year. Parkinson's disease affects more than 1 million people in North America and 7 million-10 million people worldwide.

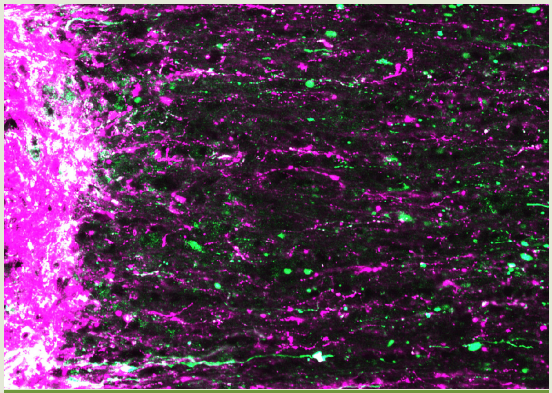
Visual Activity Regenerates Neural Connections Between Eye, Brain

An NIH-funded study in mice shows for the first time that high-contrast visual stimulation can help damaged retinal neurons regrow optic nerve fibers, otherwise known as retinal ganglion cell axons. In combination with chemically induced neural stimulation, axons grew further than in strategies tried previously. Treated mice partially regained visual function. The study also demonstrates that adult regenerated central nervous system (CNS) axons are capable of navigating to correct targets in the brain. The research was funded through the National Eye Institute.

"Reconnecting neurons in the visual system is one of the biggest challenges to developing regenerative therapies for blinding eye diseases like glaucoma," said NEI director Dr. Paul Sieving. "This research shows that mammals have a greater capacity for central nervous system regeneration than previously known."

The researchers induced optic nerve damage in mice behind one eyeball. The mice were then placed in a chamber several hours a day for 3 weeks where they viewed high-contrast images—essentially changing patterns of black lines. The mice had modest but significant axonal regrowth compared to control mice that did not receive the high-contrast visual stimulation.

"We saw the most remarkable growth when we closed the good eye, forcing the mice to look through the injured eye," said Dr. Andrew Huberman of Stanford University School of Medicine's department of neurobiology, lead author of the report published online July 11 in *Nature Neuroscience*. In 3 weeks, the axons grew as much as 12 millimeters, a rate about 500 times faster than untreated CNS axons.



Regenerating mouse retinal ganglion cell axons (magenta and green) extending from site of optic nerve injury (l)

PHOTO: ANDREW D. HUBERMAN

The regenerating axons also navigated to the correct brain regions, a finding that Huberman said sheds light on a pivotal question in regenerative medicine: "If a nerve cell can regenerate, does it wander or does it recapitulate its developmental program and find its way back to the correct brain areas?"

Devices

CONTINUED FROM PAGE 1

NIBIB-funded researchers are taking the latest technological developments and adapting them to smaller, simpler, faster, more affordable and more portable devices that can fit in a physician's office or in low-resource settings and return results in minutes.

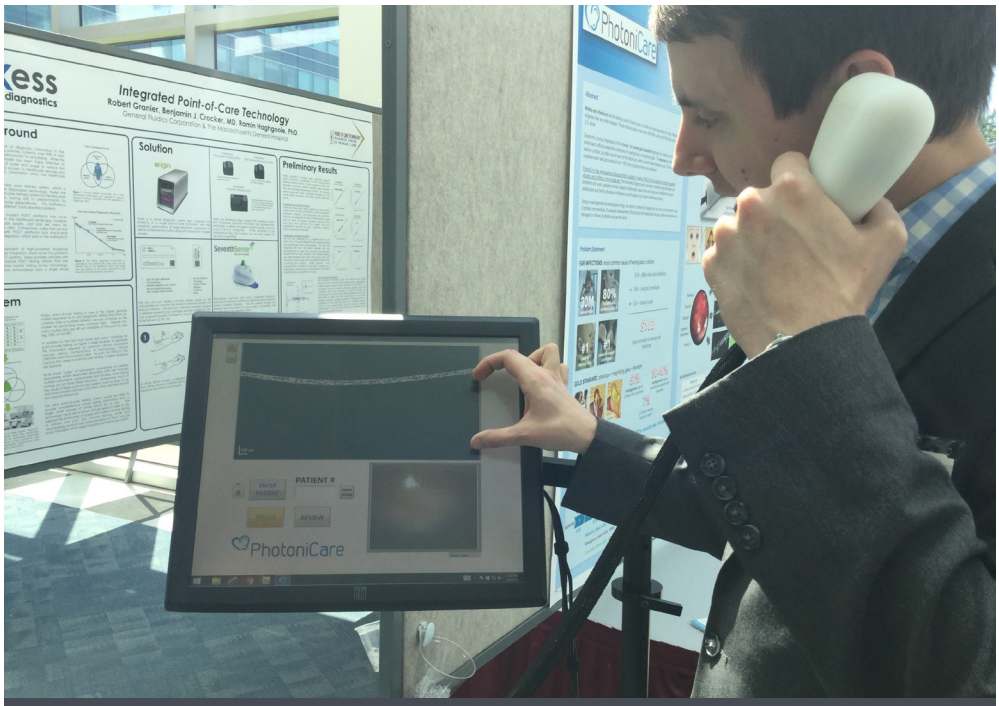
These researchers, from three different centers supported by the National Institute of Biomedical Imaging and Bioengineering, gathered at NIH this summer at the Point-of-Care Technology Research Network (POCTRN) Symposium. They shared data and ideas focusing on "Co-Inventing the Future Through Collaboration."

Speakers discussed the newest technologies that have been developed, produced and commercialized through this collaborative network, emphasizing the importance of bringing together clinicians, researchers and those with industry experience. Posters and demonstrations of technologies funded by this network gave attendees the chance to see how effective and far-reaching the POCTRN coalition has been.

One of the newest companies to develop from POCTRN funding is PhotoniCare. Ear infections are misdiagnosed up to 50 percent of the time, which means that some people—mainly children—are taking unnecessary antibiotics, while others are not receiving the treatment they need, thus increasing their chances of needing surgery in the future.

Current technology only helps doctors see the surface of the eardrum, but not the underlying middle ear where the disease resides. PhotoniCare has developed a new device that uses an advanced light technology called optical coherence tomography to see through the eardrum into the middle ear. The device has a clear black and white display that more objectively shows whether or not there is an infection by providing quantitative metrics about the infection and could greatly increase physicians' diagnostic accuracy.

Other developments include a handheld device that uses the same technology utilized in Lasik eye surgery to determine an individual's eyeglass prescription and a small toaster-sized device that can more quickly and accurately diagnose sexually transmitted infections and health care-associated infections such as chlamydia and MRSA, respectively.



Above, the PhotoniCare device shows both the eardrum and the middle ear, making it easier for physicians to diagnose ear infections. Below, the ATLAS device is small enough to fit in a physician's office or at a pharmacy and can diagnose infections such as chlamydia and MRSA in minutes.

In addition to providing funding for new technology, a center within POCTRN—the Center for Integration of Medicine and Innovative Technology—also provides essential training in accelerating the emergence of health care innovations from academic labs into commercialization and clinical practice. Commercialization Readiness Assessment and Accelerator for Solutions in Health Care is a 10-week course that helps researchers learn about the necessary steps to move their product from the lab into the market and matches the teams with experienced business mentors.

"Having an experienced personal mentor providing guidance through the customer discovery and commercialization process was extremely valuable to us," said Ryan Nolan of PhotoniCare. "This unique relationship provided us a level of exceptional support unlike the other accelerator programs we've benefitted from."

"This symposium shows just how much can be accomplished in a short time when experts from various areas work together to focus on creating and improving technology," said Dr. Tiffani Lash, director of the NIBIB programs in sensors and telehealth. "Point-of-care devices are already in high demand around the world and will continue to be needed in low-resource settings. Networks like POCTRN can help stimulate research and provide resources for new businesses to succeed."

Axelrod Symposium Showcases Neuropharmacology Research

This year's Julius Axelrod Symposium was held to honor the recipient of the 2014 Society for Neuroscience (SfN) Julius Axelrod Prize—Dr. Susan Amara, scientific director at NIMH.

The event opened with a "Remembrance of Julie" given by former NIMH intramural researcher and Axelrod mentee Dr. Michael Brownstein, who reminisced about his years with Julie, as his colleagues affectionately called him.

Dr. Michael Brownstein and Dr. Susan Amara

Often called the father of neuropharmacology, long-time NIH researcher Dr. Julius Axelrod nearly missed out on a career in science. After being rejected by medical schools, he accepted a job as a lab technician. It was as a "technician" that he conducted his early work on caffeine, which led to his later research on the sympathetic nervous system and its major neurotransmitters epinephrine (adrenaline) and norepinephrine (noradrenaline), and eventually the 1970 Nobel Prize.

In her keynote address, Amara said that Axelrod's scientific contributions while at the NIMH Intramural Research Program inspired her to join NIMH. She explained that her lab was the first to clone the human norepinephrine and dopamine transporters, which—along with the serotonin transporter—appear to be key targets for treatments of neuropsychiatric disorders and addiction.

She credits her success in part to Axelrod's support: "Dr. Axelrod wrote us a letter, gave us some advice and sent us some papers."

Amara's early work advanced understanding of how proteins shuttle signaling neurotransmitters back and forth across neurons' cellular membranes. More recently, her studies of psychostimulants and antidepressants have helped to elucidate how these agents affect neurotransmitter-transporter signaling properties, physiology and regulation.

In addition, Amara has trained more than 30 graduate students and postdoctoral fellows and held numerous leadership positions in professional societies.

"I always liked it that Julius Axelrod followed an unconventional path," she noted. "He got his Ph.D. in his 40s after working in a lab for years. It is a lesson that there are many different paths to a career in science. And it is an encouraging story for students—and for the rest of us."

NIMH visiting fellow Dr. Qin-Hua Gu, who won the 2015 NIMH IRP Fellows' Axelrod Award, spoke on specific miRNAs she has helped to identify as essential for maintaining neuronal plasticity in learning.

The 9th annual Julius Axelrod Symposium will be held at NIH in the spring of 2017 to honor the 2015 Julius Axelrod Prize awardee Pietro De Camilli, chair of the department of cell biology at Yale University School of Medicine, and the 2016 recipient, who will be announced at the annual SfN meeting in San Diego this November.

Marilyn Weiner displays a plaque recognizing her 30 years of service to NIH as a volunteer on institutional review boards.

PHOTO: RICH MCMANUS

Volunteer Weiner Ends 30 Years of IRB Service

Marilyn Weiner attended her final NIH Intramural Research Program IRB (institutional review board) meeting on June 22, ending 30 years of volunteer service to NIH. As a non-scientist and non-NIH affiliated IRB member, Weiner brought to the IRB the community and participant perspective, which is key to effective review. She is the longest serving member on any of the combined neurosciences (CNS) IRB panels and among the longest at NIH overall—she has rarely missed a monthly meeting.

Weiner originally joined the NIDCR IRB back in 1986, at the invitation of a friend. At the time, she had never heard of an "IRB" but was eager to learn about the process. She subsequently outlasted five IRB chairs over the years of her service—and can still name each one. She also persisted through 2012, when NIDCR joined the CNS IRB leadership and switched from reviewing protocols solely from NIDCR to a broad portfolio of neuroscience-related research from multiple ICs.

She has witnessed a number of other changes at NIH and in the IRB over the years. At NIH, she noted the drastic increase in security, particularly after 9/11. She appreciated that NIH intramural IRBs have become more professional as well. She found that increased IRB support from the institutes and the addition of dedicated, trained IRB professional staff were very helpful in her role as an IRB member.

Her favorite part of the IRB experience has been all that she learned. She particularly enjoyed the "informational items," such as articles about IRBs, ethics and human subjects protections issues provided by the IRB leadership at each meeting. She will miss her fellow board members.

Over the years, Weiner has managed to balance her dedication to NIH with her career as a marriage and family therapy and addictions therapist. In addition, she is the mother of 3 and the grandmother of 6.

"Ms. Weiner has been a valuable member of the NIH Intramural Research Program's NIDCR and, subsequently, CNS IRB," said NINDS's Dr. Pamela Kearney, deputy chair of the CNS IRB. "She will be greatly missed."

NINDS Mourns Scientist Emeritus Brady

BY SHANNON E. GARNETT

Dr. Roscoe Owen Brady, scientist emeritus and retired chief of the Developmental and Metabolic Neurology Branch, NINDS, died on June 13 after a long battle with cancer. He was 92 years old.

Brady was a pioneer of modern medicine. For more than 50 years, he conducted research on hereditary metabolic storage diseases, also called lipid or lysosomal storage disorders (LSDs) such as Gaucher disease, Niemann-Pick disease, Fabry disease and Tay-Sachs disease. His work defined much of what is known about the biochemistry, enzymatic bases and metabolic defects of these disorders. He inspired colleagues throughout the world to define the causes of many other related disorders and to pursue further investigations in the field of metabolic neurology.

Born in Ambler, Pa., in 1923, Brady attended Pennsylvania State University and earned his medical degree from Harvard Medical School in 1947.

After graduating, he interned at the Hospital of the University of Pennsylvania and later became a National Research Council fellow and a Public Health Service special fellow in the department of biochemistry at the University of Pennsylvania School of Medicine. He worked with Dr. Samuel Gurin, a biochemist, on research using radioactive isotopes to study the biosynthesis of testosterone, fatty acids and cholesterol.

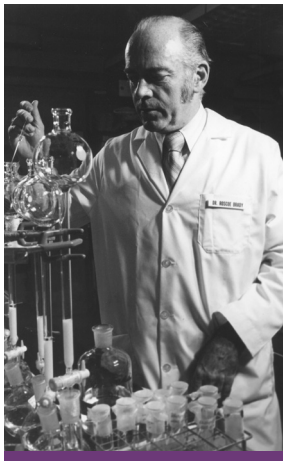
One of Brady's early scientific contributions was discovering the role of gonadotrophin on testosterone synthesis. This work not only spurred his desire to do research, but would eventually lead to his interest in lipid storage diseases.

In 1952, Brady was called to active duty in the Korean War and, for 2 years, served in the U.S. Naval Medical Corps at the National Naval Medical School in Bethesda as officer-in-charge of the department of chemistry.

Brady was recruited by Dr. Seymour Kety in 1954 to join NINDB (now NINDS) as chief of the section on lipid chemistry in the Laboratory of Neurochemistry. Kety wanted to establish a research program focused on myelin—the lipid coverings of nerves—and he knew of Brady's research at Penn. Brady would remain with NINDS for his entire career, later becoming chief of the Developmental and Metabolic Neurology Branch and eventually retiring in 2006.

While there is a great deal of research on LSDs today, there was virtually none before Brady's investigations at NIH.

In addition to identifying the enzymatic bases, he and his research team developed diagnostic tests, carrier identification procedures and methods for prenatal detection of these disorders that provided the basis for genetic counseling to at-risk families. In 1991, they established the first effective treatment—enzyme replacement therapy—for Gaucher disease.



Brady in his lab, circa 1975

"As soon as we identified the missing enzyme in Gaucher disease and Niemann-Pick disease, I thought about enzyme replacement therapy," said Brady in a 2008 interview. "Although it took many years to bring enzyme therapy to fruition, the ultimate benefit was amazing. It showed the way enzyme replacement therapy can work for human diseases."

His studies on Gaucher disease and success with enzyme replacement therapy led to breakthroughs in other areas of LSD research, including a treatment for Fabry disease and the identification of new types of LSDs.

By taking their discoveries from bench to bedside, Brady and his team brought enormous relief to patients, who without treatment suffer from a wide range of symptoms including liver and spleen enlargement, severe anemia, thrombocytopenia (low blood platelet count) and painful skeletal deformities.

"Dr. Brady's work with enzyme replacement therapy launched an important part of the biotech and pharmaceutical industry and it brought effective treatment to patients who had none," said Dr. Kenneth Fischbeck, chief of NINDS's Neurogenetics Branch. "I remember meeting with him when I first came to the NIH and he showed me pictures above his desk of patients who would not have been alive if not for the treatment he helped to develop. That's a worthy goal for all of us who are still working to fulfill the promise of safe and effective therapy for patients with hereditary diseases."

In 2002, NINDS held a 2-day symposium to honor Brady's research career. The meeting, which gathered top scientists to discuss past accomplishments and future directions of hereditary metabolic disorders research, celebrated the remarkable progress that has been made in understanding and devising therapies for these disorders and recognized Brady for his leadership.

At the time he retired, he had served as chief of the branch for 34 years. His work, however, continued as he transitioned to an emeritus role in the institute. Even after retirement, he kept searching for other ways to treat LSDs, including looking at molecular chaperone therapy—which provides a template to guide and stabilize the abnormal enzyme—and at gene therapy as a possible cure. He maintained an office adjacent to the NINDS Surgical Neurology Branch.

"Dr. Brady biked or drove his convertible to NIH at least 3 days per week," said SNB chair Dr. John Heiss. "He worked all day, keeping up with developments in the field of LSDs and becoming an expert in the biochemistry of tumorigenesis. His office door remained open and through it passed all levels of scientists, from principal investigators to IRTAs. They left his office with scientific insights, manuscript editing and valuable mentorship. His keen intellect defied the aging process."

Throughout his career Brady received numerous accolades: the Lasker Foundation Award (1982), the Kovalenko Medal from the National Academy of Sciences (1991) and the Alpert Foundation Prize from Harvard Medical School (1992).

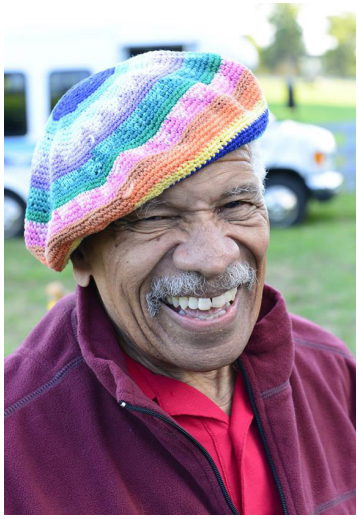
In 2008, he received the National Medal of Technology and Innovation, the highest

honor for achievement in science and technology bestowed by the President of the United States. He had been nominated several times for the Nobel Prize in medicine or physiology by other Nobel laureates.

Brady published hundreds of research articles and authored or co-authored nearly 50 scientific manuscripts after "retiring." He trained many doctors and, until recently, regularly attended and contributed to NINDS grand rounds and scientific conferences. He served on editorial and advisory boards for many journals and organizations and was an adjunct professor at Georgetown University School of Medicine.

Brady was a member of the National Academy of Sciences and the National Academy of Medicine. His work is featured on the NIH Office of History web site, www.history.nih.gov/exhibits/gaucher/index.html.

Brady is survived by his wife Bennett, sons Roscoe Jr. and Owen, and granddaughters Elinor and Beatrice.



Rec Therapist, Volunteer Butler Dies

Charles Delmus Butler, 81, a retired recreation therapist at the Clinical Center and long-time campus volunteer, died June 13 after battling multiple cancers over the past few years.

A native of Maryland's Eastern Shore who was born near Chestertown, Butler graduated from Morgan State University and earned his master's degree in recreation therapy from George Washington University.

He spent 18 years in recreation with the D.C. government, where he was first director of the D.C. Therapeutic Recreation Center in southeast Washington. He then came to the Clinical Center's department of rehabilitation medicine, where he worked for 30 years before retiring in 2006.

He was an active member of many clubs, organizations and charities at NIH, including serving as a volunteer and on the boards of the Recreation & Welfare Association and its foundation. He was also involved with Special Love, Inc., which sponsors Camp Fantastic, a summer camp for children with cancer, for all of its 35-year history, and Friends of Patients at the NIH.

Up until the end of his life, Butler was an active volunteer for R&W programs including the Camp Fantastic BBQ and NIH Night at the Circus. He was also an avid globetrotter who accompanied the NIH Ski and Travel Club on many trips around the world, including the club's 2015 African Safari, which he refused to miss despite being treated for cancer.

An avid cyclist, Butler regularly completed 20-mile bike rides until 2 months before his passing.

"NIH was lucky to have had Charles," said Randy Schools, retired CEO of R&W. "He had all of the attributes of what is known as a good person—kindness, loyalty, joy, wisdom, tolerance and compassion. That is what Charles gave us, comfort and care. The strength he brought to the NIH community is immense."

"Charles was a true *mensch* in every sense of the word," said his CC colleague Debbie Marcus. "His life of service and humility was second to none and he will be missed more than words can say."

"No one was more committed to helping others than [Butler]," said David Browne of R&W. "The stories of all he's done for the children with cancer at NIH, his friends, his family and so many others—you'd think he was a saint."

Butler is survived by his wife Nancy, his children Larry, Cheryl and Dennis, sisters Hilda Hopkins, Doris Woodus and Elaine Roberts, and brothers William Butler and Edward Butler.

Donations in his honor can be made to Special Love Inc., and can be left at the R&W store in Bldg. 31. Proceeds will go towards planting cherry trees at Camp Fantastic in his memory.

Study Seeks Healthy Older Adults

Healthy older adults, ages 55-70, are invited to participate in an outpatient research study investigating the benefits of tart cherry and aroniaberry supplementation on vascular health. The goal of the study is to determine whether the supplements improve blood flow and blood vessel function that can affect your heart. Eligible participants must be medication-free and in good general health. The study will be carried out in an outpatient clinic and includes 7 visits over 3-4 months. Compensation for the study is provided. For more information, call 1-800-411-1222 (TTY 1-866-411-1010) and refer to study 15-NR-0085.

Study Seeks Older Adults

Healthy older adults ages 55-75 are invited to participate in an outpatient research study investigating the benefits of omega-3 oil and blackcurrant supplements on vascular health. The goal of the study is to determine whether the supplements improve blood flow and blood vessel function that can affect your heart. Eligible participants must be medication-free and in good general health. The study will be carried out in an outpatient clinic and includes 4 visits over 6 months. Compensation is provided. For more information, call 1-800-411-1222 (TTY 1-866-411-1010) and refer to study 14-NR-0034.

NIAID in Search of Healthy Volunteers

NIAID study seeks healthy adult volunteers, 18-64 years old. Researchers want to better understand the effects of glucocorticoids on the body. These medications are commonly used to treat conditions that cause inflammation on the skin and in the body like lupus, asthma and eczema. This research may help us find better treatments for people with conditions that cause inflammation. Participants will receive one intravenous dose of a glucocorticoid and a glucocorticoid cream will be applied to a small area of the skin. Blood and skin samples will be collected. Two outpatient visits at the Clinical Center are required. Compensation is provided. For more information, contact the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Refer to study 16-I-0126.

NIMH Recruits Healthy Volunteers

NIMH is studying how two commonly prescribed medications affect attention and anxiety while a person is performing computer-based tasks under stress. Researchers are seeking healthy volunteers, 18-50 years old without mental health disorders. Study requires 2 outpatient visits to the Clinical Center. Compensation will be provided. For more information, call (301) 451-5087 or email bari.fuchs@nih.gov. Refer to study 14-M-0114.

Collins, Band Rock for Fellows on South Lawn

PHOTOS: ERNIE BRANSON

On July 5, hundreds of NIH staff, fellows and guests outside Bldg. 10's south entry may have been pleasantly surprised by the sight of a full rock and roll band, complete with dancers. But these were no regular musicians, lost on their way to Bonaroo; this was NIH's own multi-talented band, the Affordable Rock 'n' Roll Act (ARRA), formerly known as The Directors.

To celebrate the contributions of NIH fellows, frontman NIH director Dr. Francis Collins, clad in all black, jammed with nine scientists and physicians from NIAMS, NHGRI, NCI, NHLBI and NIAID. The band performed rock, blues and Motown tunes spanning multiple decades. Collins even wrote a song for the occasion, to the tune of Three Dog Night's *Joy to the World*.

Some NIH'ers, such as NLM visiting scientist Donald Ekong, knew about the event in advance. "I'm a groupie by nature," he said. "This is great!"

Others happily stumbled upon the concert. NIMH fellow Sunny Jiang heard the music from her office in Bldg. 49 and came down to check it out. "I thought Dr. Collins only played country music," she exclaimed. "He's playing rock!"

ORF's Mike Moore strolled by with his intern Andre on his first day at NIH. "So now Andre thinks it's a party here every day," joked Moore. "But really, they should do this more often. It's a great way to break up the day."

The concert, sponsored by the visiting fellows committee, the Office of Research Services and the Recreation & Welfare Association, was located next to the weekly NIH Community Market. Concertgoers took advantage of the food while enjoying the music.

After 90 minutes of spirited playing, the band left the stage. Chanting, "One more song!" the crowd couldn't get enough. Not wishing to disappoint their fans, the band happily complied.

To see clips from the concert, visit https://www.facebook.com/NIHRW/.—**Courtney Bell, Dana Talesnik**

Above, as ARRA members (from l) Dr. John O'Shea, Quino Maduro, Cassie Parks, Dr. Robert Walker, Dr. John Tisdale, Dr. Peter Grayson, Dr. Mike Lenardo, Dr. Mike Pazin, NIH director Dr. Francis Collins and Dr. Scott Durum play, dancers Dr. Ronald Germain and his wife Gale dance to the music. Below, the audience included kids and adults. At right, from top down, are singers Maduro and Parks; Collins, a multi-instrumentalist, on keyboard; and guitarist Grayson. Most of the band has played together before in various configurations. In fact, O'Shea has performed with Collins for decades. One new and much-talked-about addition was NIAMS postbac fellow Parks, who, in addition to singing, played violin and xylophone.